REMARKS

Favorable reconsideration of this application is requested. Claim 1 has been revised to include the feature of claim 5, i.e. the further coating layer comprising water-soluble sugar alcohol on the enteric-coated fine granules. Claim 5 thus has been canceled without prejudice or disclaimer. Claim 1 also has been clarified editorially in light of this revision, to confirm that the water soluble sugar alcohol (ii) is separate from that of the coating on the granules. Claims 1-3, 7, 9, 11-19, 21-24, 29, 31, 50 and 51 are pending.

Claims 1-3, 5, 7, 9, 11-19, 21-24, 29, 31, 50 and 51 have been rejected as unpatentable over Lundberg in view of Watanabe. Applicants respectfully traverse this rejection.

Claim 1 is directed to an orally disintegrable tablet comprising fine granules that contain an acid-labile physiologically active substance in a relatively large amount. The fine particles have an average particle diameter of 400μm or less, which is beneficial in reducing feelings of roughness and oral discomfort when a patient takes the tablet. The production and handling of such tablets can be problematic, since the final tablet must disintegrate readily upon administration (within one minute in claim 1), but must have sufficient strength and integrity to withstand the rigors of the tabletting and subsequent handling steps. This is complicated by the presence of the acid-labile physiologically active substance, which requires that damage to the fine granules themselves be avoided to prevent exposure of the active substance to stomach acid after administration.

Claim 1 requires the presence of a sugar alcohol coating on the enteric coated granules, which is separate from other sugar alcohol contained in the product. This feature is advantageous in promoting the hardness of the tablet, thereby permitting the production of a tablet that can withstand the tabletting and handling steps without increasing the likelihood of damage to the fine granules themselves. See page 30, lines 7-11 of the present specification. Applicants have conducted an experimental comparison showing that tablets prepared with granules that were overcoated with the sugar alcohol mannitol showed a hardness that was increased by nearly 50% relative to that of corresponding tablets prepared with granules that did not have the mannitol overcoating (6.8 kg vs. 4.8 kg). A Declaration describing the experiments in more detail will be submitted shortly.

Neither Lundberg nor Watanabe suggests the presence of the sugar alcohol coating on the granules. Watanabe is silent about such coatings. Lundberg merely indicates generally that the

overcoating materials can be chosen from a variety of materials including sugar, polyethylene glycol, polyvinylpyrrolidone, polyvinyl alcohol, polyvinyl acetate, hydroxypropyl cellulose, methylcellulose, ethylcellulose, hydroxypropylmethylcellulose, carboxymethylcellulose and others. See Col. 11, lines 3-9. Hydroxypropylmethylcellulose is used in the examples. Therefore, even when combined the reference disclosures fail to meet the requirements of claim 1. Nor does either reference suggest any reason to expect the increased tablet hardness for a tablet that still maintains suitable oral disintegration properties that can be achieved through the use of the sugar alcohol coating on the tablets. Therefore, the present invention is not suggested by the references.

Moreover, Applicants respectfully maintain that the present record does not justify the combination of the reference disclosures absent the impermissible use of Applicants' own disclosure as a guide to making the combination. Lundberg is directed to effervescent tablets. These tablets are intended to be dispersed in a liquid such as drinking water prior to administration to the patient. In contrast, Watanabe is directed to a dosage from that disintegrates readily in the mouth. While the two share the general objective of providing a dosage form that is useful for patients who have trouble swallowing, the administration conditions between the two differ radically in terms of the nature, viscosity and volume of the fluid involved. That is, Lundberg is concerned with promoting a relatively uniform dispersion in a relatively large volume of low viscosity liquid that the patient intakes by drinking. In contrast, the orally disintegrable tablet is intended to disintegrate through interaction with the relatively small amount of relatively viscous saliva in the patient's oral cavity. The Shimizu Declaration filed with the March 20, 2006 response in this application demonstrates that the Lundberg compositions in fact do not show good oral disintegration properties. Nothing in the present record shows any reason to expect that Watanabe's measures directed to orally disintegrable products would have any relevance to the effervescent products of Lundberg. Given the demonstration of the inadequate oral disintegration properties of Lundberg's product, there likewise would be no reason to apply those teachings to Watanabe's orally disintegrable products. Therefore, Applicants maintain that the present record does not even establish prima facie obviousness for the present invention.

In view of the above, Applicants request reconsideration of the application in the form of a Notice of Allowance.

Respectfully submitted,

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